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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,000	09/26/2003	Anne Skaja Robinson	00131-00350-USU	9773
23416 7590 06/11/2007 CONNOLLY BOVE LODGE & HUTZ, LLP P O BOX 2207 WILMINGTON, DE 19899			EXAMINER STEELE, AMBER D	
			ART UNIT 1639	PAPER NUMBER
			MAIL DATE 06/11/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/673,000	<b>Applicant(s)</b> ROBINSON ET AL.	
	<b>Examiner</b> Amber D. Steele	<b>Art Unit</b> 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on November 2, 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.  
     4a) Of the above claim(s) 13-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 3-5, 7-8, 10-11 is/are rejected.
- 7) ☒ Claim(s) 2, 6, 9 and 12 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03/03/04 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

1. Please note: the examiner of record for the present application has changed. However, the Technology Center (TC1600) and Art Unit (AU1639) remain the same.

#### ***Status of the Claims***

2. The amendment to the claims received on November 2, 2006 amended claims 3, 5, 8, 11, 14, and 17.

Claims 1-18 are currently pending.

Claims 1-12 are currently under consideration.

#### ***Election/Restrictions***

3. Claims 1-6 are linking claims. Applicants elected Group I (Claims 7-12) in the reply filed on March 28, 2006 without traverse. Thus, claims 13-18 are withdrawn from consideration as being drawn to a non-elected invention.

#### ***Response to Amendment***

4. The declaration under 37 CFR 1.132 filed November 2, 2006 is sufficient to overcome the denial of priority for claims 3-68, and 10-12 and the objection to the specification due to the showing by applicants of the support for the various claim limitations.
5. The declaration under 37 CFR 1.132 filed November 2, 2006 is sufficient to overcome the 35 USC 112, first paragraph rejections of claims 1-6 due to the knowledge in the prior art regarding protein denaturation and aggregation.

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6. The declaration filed on November 2, 2006 under 37 CFR 1.131 is sufficient to overcome the Randolph et al. reference.

***Priority***

7. This instant application is a DIV of 09/695,762 filed 10/25/2000, which claims benefit to a provisional application of 60/161,035 filed 10/25/1999.

8. Applicants arguments and the declaration submitted by Dr. Robinson on November 2, 2006 were persuasive in determining that claims 1-12 have a priority date of October 25, 1999.

***Invention as Claimed***

9. The instant invention recites a method for recovering native protein from a sample. The method comprises the steps of a) obtaining a sample comprising protein aggregates; b) subjecting the sample of step (a) to elevated hydrostatic pressure, whereby a portion of protein dissociates from said protein aggregates; c) returning the sample of step (b) to ambient pressure, wherein a portion of the dissociated protein refolds to native protein and variations thereof.

***Withdrawn Objections***

10. The objection to the specification regarding antecedent basis for the claimed subject matter of claims 3-6, 8, and 10-12 is withdrawn in view of the declaration submitted by Dr. Robinson on November 2, 2006 and applicants' persuasive arguments.

11. The objection to claims 3, 5, 8, and 11 regarding the term "hydrostic" instead of hydrostatic is withdrawn in view of the amendment to the claims received on November 2, 2006.

**Objection Necessitated by 37 CFR § 1.131**

***Claim Objections***

12. Claims 2, 6, 9, and 12 are objected to as being dependent upon a rejected base claim, but are free of the art of record.

**Withdrawn Rejections**

13. The rejection of claims 1-12 under 35 U.S.C. 112, first paragraph (written description) is withdrawn in view applicants persuasive arguments and the declaration submitted by Dr. Robinson on November 2, 2006 regarding the level of knowledge in the prior art regarding protein denaturation and aggregation.

14. The rejection of claims 1-12 are rejected under 35 U.S.C. 112, first paragraph (scope of enablement) is withdrawn in view applicants persuasive arguments and the declaration submitted by Dr. Robinson on November 2, 2006 regarding the level of knowledge in the prior art regarding protein denaturation and aggregation.

15. The rejection of claims 3-5, 8, 10, and 11 under 35 U.S.C. 112, second paragraph, as being indefinite regarding the limitations “*wherein said elevated hydrostatic pressure is insufficient to fully denature said protein*”, “*elevated hydrostatic pressure*”, “*wherein said elevated hydrostatic pressure is insufficient to fully denature said protein*”, “*a chaotropic agent in an amount which is insufficient to denature said native protein at ambient pressure*”, “*amount*”, and “*a chaotropic agent in an amount which is insufficient to denature said native protein at ambient pressure*” is withdrawn in view applicants persuasive arguments and the

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declaration submitted by Dr. Robinson on November 2, 2006 regarding the level of knowledge in the prior art regarding protein denaturation and aggregation.

16. The rejection of claims 1-12 under 35 U.S.C. 102(e) as being anticipated by Randolph et al. (US Patent 6,489,450 B2; priority date of July 9, 1998) alone or as evidenced by Paladini et al. (*Biochemistry*, **1981**, 20(9), pgs. 2587-2593) are withdrawn in view of the declaration swearing behind the July 9, 1998 priority date of Randolph et al.

#### **Maintained Rejection**

17. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Claim Rejections - 35 USC § 102***

18. Claims 1, 3-5, 7, 8, 10, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Gorovits et al. (*Biochemistry*, **4/28/1998**, 37(17), pgs. 6132-6135).

Gorovits et al. demonstrate that high pressure can increase protein folding by reducing nonspecific aggregation (see Abstract; pg. 6132, right col., lines 9-13; pg. 6133, left col., lines 29-40). The method comprises the step of preparing a sample of native rhodanese in 3.9 M concentration of urea (refers to instant claimed chaotropic agent) wherein rhodanese forms a molten globule-like structure that has a high level of hydrophobic exposure and a considerable amount of secondary structure (refers to instant claimed protein aggregates comprising protein folding intermediates; instant claimed step (a) for claims 1 and 7; and instant claims 4, and 10); subjecting the rhodanese sample to pressure at 2 kbar such that protein intermediates precipitates, i.e. dissociates, (refers to instant claimed step (b) for claims 1 and 7; and instant claims 3, 5, 8,

and 11); and reducing the pressure such that the rhodanese are refolded to its native form (refers to instant claimed step (c) for claims 1 and 7)(see e.g. pg. 6133, left col., lines 29-40; pg. 6133, right col., lines 4-8; pg. 6133, right col., line 26 thru pg. 6134, left col., lines 3; pg. 6134, left col., lines 12-15; pg. 6134, right col., lines 17-33). Therefore, the method of Gorovits et al. anticipates the presently claimed method.

### *Arguments and Response*

19. Applicants' arguments directed to the rejection under 35 USC 102 (b) as being anticipated by Gorovits et al. for claims 1, 3-5, 7, 8, 10, and 11 were considered but are not persuasive for the following reasons.

Applicants contend that Gorovits et al. do not teach method step (c) wherein the sample is returned to ambient pressure and the protein refolds to native protein.

Applicants' arguments are not convincing since the teachings of Gorovits et al. anticipate the method of the instant claims. Gorovits et al. teach that "after unfolding, the protein was diluted to 3.6 µg/ml and allowed to refold for the indicated time in the presence of 200 mM βME, 50mM sodium thiosulfate, and 50 mM Tris-HCL, pH 7.8...[t]he regain of enzyme activity was used to monitor successful refolding" (please refer to page 6133, left column, lines 43-48). In addition, Gorovits et al. teach that "[r]hodanese undergoes an unfolding transition when subjected to increasing concentrations of urea...[a]t intermediate urea concentrations, rhodanese forms a molten globule-like structure" (please refer to paragraph spanning pages 6132 and 6133). Thus, in order for the protein to refold and regain enzyme activity a urea concentration of 3.9 M can not be present (i.e. concentration of urea wherein rhodanese forms a molten globule-like structure). Furthermore, Gorovits et al. teach that "[p]rotein was initially unfolded at 6 M

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urea...[a]fter dilution into the refolding buffer, pressure was adjusted up to 2 kbar after 6 min of incubation". Thus, Gorovits et al. utilized a refolding buffer (e.g. either without urea or to dilute the urea present to concentrations insufficient for denaturation) for the refolding of the protein (please refer to page 6135, left column, lines 1-4).

### ***Conclusion***

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

### ***Future Communications***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ADS

May 31, 2007

A handwritten signature in black ink, appearing to read 'Mark L. Shibuya', with a stylized, sweeping flourish at the end.

MARK L. SHIBUYA  
PRIMARY EXAMINER